CONCISE COMMUNICATION

Recurrent catheter-related *Rhodotorula rubra* infection

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A 34-year-old male receiving chronic parenteral nutrition for treatment of short bowel syndrome and intermittent immunosuppressive agents for juvenile rheumatoid arthritis developed recurrent, catheter-associated *Rhodotorula rubra* fungemia over a one-year period. Infection with this yeast is associated with insertion of central venous catheters. Recurrence of *R. rubra* infection is an unusual event that presumably occurred because of chronic skin colonization by the organism.

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A 34-year-old man with juvenile rheumatoid arthritis and short bowel syndrome, who was receiving total parenteral nutrition through a Hickman catheter, presented to our hospital in October 2001. The patient had a prior history of *Rhodotorula rubra* Hickman catheter-associated infection in October 2000. At that time, he noted progressive fatigue and several episodes of chills without fevers. The rheumatoid arthritis had been active over the previous eight months, requiring administration of oral corticosteroids, cyclosporin, and plaquenil, but his symptoms were not consistent with typical flares. Blood cultures (Bactec 9240, Becton Dickinson, Sparks, MD, USA), obtained on an outpatient basis through the Hickman catheter and from a peripheral site, yielded budding yeast from the catheter-drawn culture only. The patient was subsequently admitted to the hospital.

Physical examination was remarkable for the presence of thrush and synovial thickening of the joints of both wrists and hands. There was no tenderness or erythema at the Hickman catheter exit site. Fundoscopic examination showed no evidence of retinal involvement. The white blood cell (WBC) count was 5700/mm^3 (55% neutrophils, 35% lymphocytes). At the hospital, blood was again drawn from the catheter and a peripheral site, and inoculated into Bactec blood culture bottles. Yeast was subsequently identified from the aerobic bottle of the set taken through the catheter. The yeast was subcultured on Sabouraud–dextrose agar (Remel, Lenexa, KS, USA) and incubated at 30 °C. Salmon-pink mucoid colonies were isolated after 72 h (Figure 1). We subsequently tested the isolate with the RapID Yeast Plus System (Innovative Diagnostic Systems, Norcross, GA, USA), and it was identified as *R. rubra* (Microcode number 542044). The Hickman catheter was surgically removed, and the tip was cultured. No signs of infection were noted at the time of surgery. The Hickman catheter tip grew *R. rubra*. Repeat peripheral blood cultures after Hickman catheter removal remained negative. Antifungal susceptibility testing was not performed. The patient was discharged from the hospital on fluconazole 400 mg daily for ten days through a peripherally inserted central catheter, and he improved clinically over the next week. His peripherally inserted central catheter was removed after completion of antifungal therapy, and a new Hickman catheter was surgically implanted on November 2000.

The patient remained well until October 2001, when he again developed weakness, malaise, and

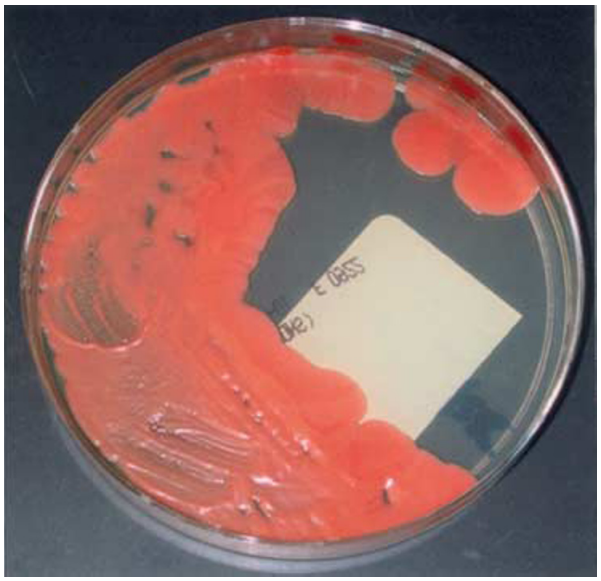

Figure 1 Subculture from Bactec blood culture bottle on Sabouraud–dextrose agar demonstrating salmon-pink colonies subsequently identified as *Rhodotorula rubra*.

chills without fever. Blood cultures drawn at home were obtained via peripheral venipuncture as well as through the catheter. Hickman and peripheral cultures grew budding yeast from the aerobic bottles of both blood culture sets, and the patient was again admitted to the hospital. Physical examination was remarkable only for tenderness at the Hickman catheter exit site. No erythema or discharge was noted. A retinal examination was normal. The WBC count was 6200/mm^3 (58% neutrophils, 32% lymphocytes). Blood cultures drawn at home and from a peripheral set at the hospital again yielded *R. rubra*. The Hickman catheter was removed, and culture of the tip also revealed *R. rubra*. A transesophageal echocardiogram was performed, and showed no evidence of vegetations on the heart valves. Another peripherally inserted central catheter was put in place, and the patient received liposomal amphotericin B (3 mg/kg/day) for two weeks. After completion of therapy, repeat blood cultures showed no fungal growth, and there has been no evidence of recurrent fungal infection.

Rhodotorula species, which belong to the family Cryptococcaceae, are generally considered to be non-pathogenic, and have rarely been a cause of infection in humans. They are ubiquitous organisms commonly recovered from human skin, lungs, conjunctivae, urine, and gastrointestinal tract, as well as from numerous environmental sources [1–3]. These yeasts also possess a strong affinity for plastics [1].

The genus *Rhodotorula* contains eight species, and *R. rubra* is the most frequently isolated from clinical specimens [2]. *Rhodotorula* species produce glistening mucoid colonies. The carotenoid pigment torularhodin [2] gives their colonies a salmon-pink to coral-red appearance on most mycologic agar media. *Rhodotorula* can be differentiated from the other red yeast, *Sporobolomyces*, by its lack of ballistospore formation. *R. rubra* and other *Rhodotorula* species resemble yeasts of the genus *Cryptococcus* in that they are round to oval-shaped, reproduce by multilateral budding, and form a capsule. *R. rubra* can assimilate various carbohydrates, including glucose, sucrose, maltose, trehalose, D-xylose, and raffinose, and is positive in tests for urease. The species does not assimilate nitrate or nitrite, and does not ferment conventional sugars. *Rhodotorula* may be differentiated from *Cryptococcus* by its inability to assimilate inositol.

The major risk factor for rhodotorula fungemia has been prolonged insertion of central venous catheters. Kiehn et al [1] reported 23 cases of rhodotorula sepsis from 1985 to 1989, and the major risk factor was the use of indwelling catheters. *Rhodotorula* typically remains in the lumen of the catheter, and peripheral blood cultures are often negative [1]. However, the presence of underlying immunologic compromise can allow the yeast to disseminate following the insertion of a central catheter. Conditions such as malignancy, prolonged neutropenia and the acquired immunodeficiency syndrome have all been associated with *R. rubra* fungemia [1]. Broad-spectrum antibiotics, corticosteroids and hyperalimentation are also known risk factors for *R. rubra* fungemia. Both episodes of *R. rubra* infection in our patient were catheter related. The yeast was probably present on the skin, and eventually adhered to the catheter, evoking symptoms of infection that primarily manifested as malaise. As is typical in rhodotorula catheter-related infections, the initial episode was not associated with positive peripheral blood cultures. Our patient's use of immunosuppressive agents for his rheumatoid arthritis probably allowed the yeast to disseminate throughout the bloodstream during the recurrence.

Rhodotorula is increasingly being identified as a human pathogen, and over 50 cases of infection have been reported. The majority of cases comprise fungemias in patients with central venous catheters [1,4–7]. Fever is the most common clinical symptom, but isolation of *Rhodotorula* has occasionally been associated with septic shock-like states [4,7,8]. *Rhodotorula* species have also been reported to cause meningitis [9], endocarditis [8,10], endophthalmitis [11], and peritonitis in patients undergoing peritoneal dialysis [12]. In general, *R. rubra* seems to have lower virulence in comparison to other yeasts, with about 15% mortality overall [13]. However, infection can occasionally be a life-threatening complication, particularly in immunocompromised individuals. Fatal cases of rhodotorula meningitis [9] and fungemia [14] have been well documented by autopsy findings. Recurrence of *R. rubra* infection has not been previously reported. Since we were unable to obtain the initial *R. rubra* isolate that infected the patient, we could not definitively determine, using molecular techniques, that infection with the same organism recurred, but this is the most likely explanation.

The management of catheter-related rhodotorula infections remains controversial. Some investigators suggest that central venous catheter removal alone is sufficient for cure [3]. Others have demonstrated that antifungal therapy without removal of the catheter can be curative [1,5]. Finally, several authors have advocated both removal of the indwelling catheter and the use of antifungal therapy because of the occasional life-threatening complications of rhodotorula sepsis [1].

There are few reports of the susceptibility of *Rhodotorula* species to antifungal agents. Kiehn et al [1] performed antifungal susceptibility testing on nine strains of *Rhodotorula* species in their series. The isolates were most susceptible to 5-fluorocytosine (MIC < 0.1 mg/L), moderately susceptible to amphotericin B alone (MIC range $= 0.8$–1.6 mg/L), and resistant to fluconazole (MIC range $= 6.4$–100 mg/L). Amphotericin B has been the antifungal agent most commonly used for the treatment of rhodotorula infection. However, three groups have recently achieved cure using liposomal amphotericin B [6,15,16].

During our patient's initial *R. rubra* infection, removal of the Hickman catheter was probably the key intervention that produced his clinical improvement. The administration of fluconazole after catheter removal was probably not beneficial, because of the generally high fluconazole MICs of *R. rubra*. At the time of the recurrence, the presence of fungemia with multiple positive peripheral blood cultures prompted us to administer systemic antifungal therapy in addition to removing the catheter to avoid a potentially life-threatening infection. Liposomal amphotericin B was used because it is generally better tolerated than conventional amphotericin B. The appropriate duration of treatment for rhodotorula infections has not been delineated. Two weeks of therapy was chosen to ensure complete eradication of the yeast from the bloodstream, and this was 1 week longer than recommended by Kiehn et al [1].

This case represents the first report of recurrent catheter-related infection with *R. rubra*. Removal of the indwelling catheter alone may be effective, but systemic antifungal therapy should be added to prevent more serious infection.

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